



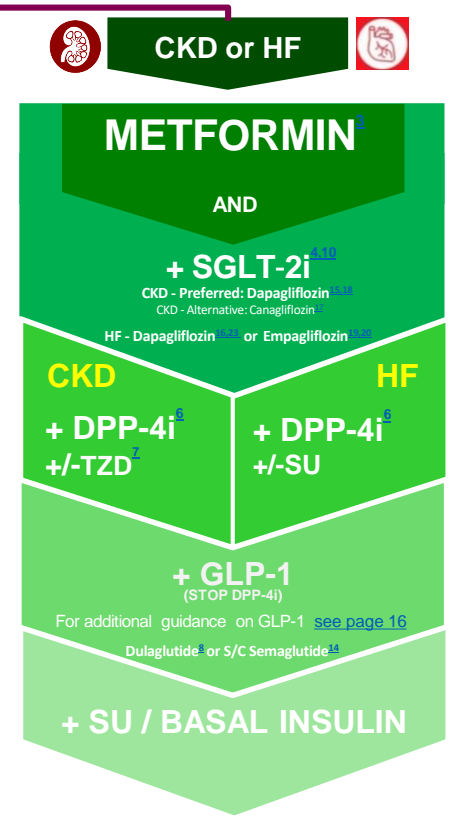
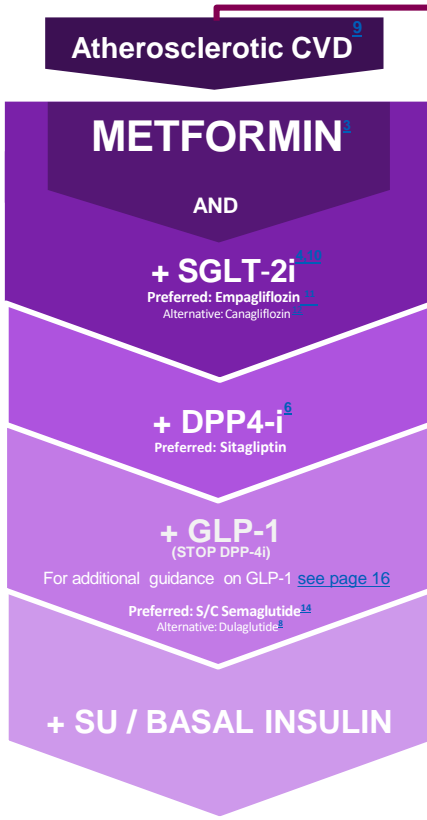
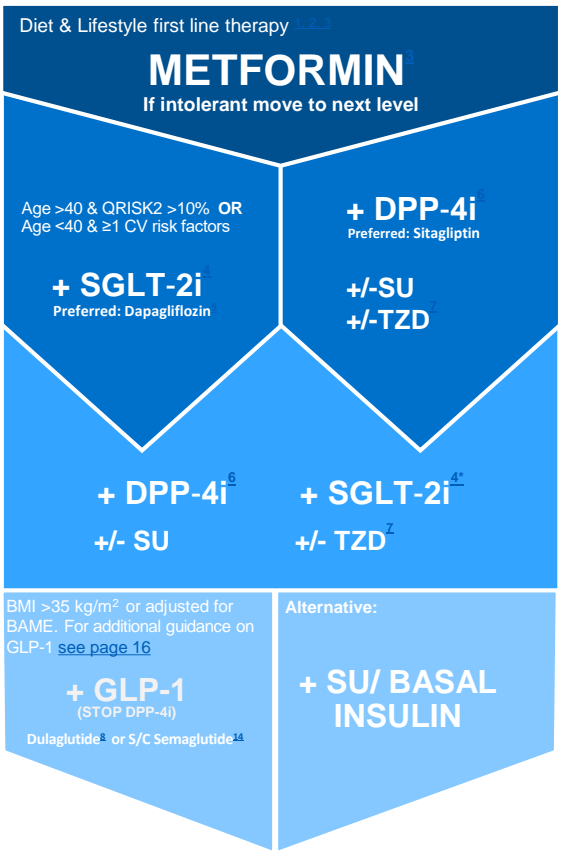
Diet & Lifestyle first line therapy ^{1,2}
Sick Day Guidance – [see page 17](#)

Does the patient have a **CARDIO-RENAL COMORBIDITY?**

NO

YES

Intensive diet & lifestyle management for all patients¹
Diabetes remission is a practical target for primary care²
Consider enrolment into REWIND Programme for either low calorie total diet replacement or low carb pathway¹



Initial therapy

Intensification if HbA_{1c}>58 or cardio-renal comorbidity

Target HbA_{1c}

Rescue therapy: Insulin or SU	Rescue based therapy if symptomatic or high HbA _{1c} Review once symptoms resolved +/- target HbA _{1c} achieved ¹
When initiating a SGLT2i	Consider a 25% dose reduction in any concomitant SU or Basal insulin & monitor for evidence of hypoglycemia
GLP-1	Only continue in those with a beneficial metabolic response after 6 months (see Additional Guidance - see page 16)

TYPE 2 DIABETES – DOSE ADJUSTMENT IN RENAL /HEPATIC IMPAIRMENT

Drug	CKD stage 1 eGFR >90 mL/min	CKD stage 2 eGFR 60-90 mL/min	CKD stage 3a eGFR 45-59 mL/min	CKD stage 3b eGFR 30-44 mL/min	CKD stage 4 eGFR 15-29 mL/min	CKD stage 5 eGFR <15 mL/min	Mild to moderate hepatic impairment	Severe hepatic impairment
Metformin	✓	✓	✓	✓ Max 500mg BD	✗	✗	Specialist initiation only	✗
Gliclazide	✓	✓	✓	✓	Use lowest effective dose		✓	✗
Linagliptin	✓	✓	✓	✓	✓	✓	✓	✓
Sitagliptin	100 mg	100 mg	100mg	50mg	25mg	25mg	✓	✗
Alogliptin	25mg	25mg	25mg	12.5mg	6.25mg	6.25mg	✓	✗
Pioglitazone (TZD)	✓	✓	✓	✓	✓	✓	✗	✗
Dapagliflozin	✓ Start 10mg	✓ Start 10mg	✓ Start 10mg	✓ Start 10mg	✓ Start 10mg	✓ Continue 10mg	✓	✓ 5mg
Canagliflozin	✓ Start 100-300mg	✓ Start 100-300mg	✓ Start 100mg	✓ Start 100mg	✓ Continue 100mg if uACR >30mg/mmol	✓ Continue 100mg if uACR >30mg/mmol	✓	✗
Empagliflozin	✓ Start 10-25mg	✓ Start 10-25mg	T2DM with eCVD ✓ Start 10mg	T2DM with eCVD ✓ Start 10mg	T2DM ✗ T2DM + HF eGFR < 20 ✗	✗	✓	✗
Ertugliflozin	✓ Start 5-15mg	✓ Start 5-15mg	✓ Start 5mg	✓ Continue 5 mg	✗	✗	✓	✗
Liraglutide	✓	✓	✓	✓	✓	✗	✓	✗
Semaglutide	✓	✓	✓	✓	✓	✗	✓	Caution: limited information
Dulaglutide	✓	✓	✓	✓	✓	✗	✓	✓
Insulin	✓	✓	✓	✓	✓	✓	✓	✓

Be Aware: Diminished glycaemic effect of SGLT-2i with eGFR < 45 mL/min, however sustained cardio-renal protection

Key ✓ Initiate ✓ No new initiation; continue at stated dose ✗ Discontinue

Treatment priority

Weight loss as a secondary benefit of glucose lowering therapy

Semaglutide subcutaneous

(once weekly)

28 days supply = 1 box of 1 pen, each pen contains four doses.

Semaglutide oral (once daily)¹³

- Use S/C Semaglutide wherever possible as greater efficacy and proven CV benefit. Oral Semaglutide should only be considered for patients who are unable to receive GLP-1 in an injectable form.
- Confirm person can adhere to the fasting administration requirement (no tea, coffee, milk, food, other medicines for 30 minutes after dosing) and an increase in total daily dosing frequency

Alternative subcutaneous preparation

Liraglutide

(once daily dose - maximum 1.2 mg)

One pre-filled pen contains 18 mg.

Primary CV risk reduction (if high risk of CVD)

Dulaglutide

(once weekly)

28 days supply = 1 box of 4 pens, each pen contains one dose.

Secondary CV risk reduction (if established CVD)

Semaglutide subcutaneous

(once weekly)

28 days supply = 1 box of 1 pen, each pen contains four doses.

Dulaglutide

(once weekly)

28 days supply = 1 box of 4 pens, each pen contains one dose.

Definitions

Established CVD:

- Evidence of prior cardiovascular event (e.g. MI/Stroke/UA),
- Prior coronary, carotid or peripheral arterial revascularisation or peripheral vascular disease
- Proven myocardial ischaemia

High risk of CVD:

- Absence of established CVD, **and**
- CVD risk factors including but not limited to:
 - coronary, carotid or lower extremity artery stenosis
 - eGFR persistently <60 mL/min/1.73 m²
 - hypertension with left ventricular hypertrophy; or persistent albuminuria

NICE Recommendation for GLP-1 agonist therapy²¹ Starting & Dose Titration:

If triple therapy with metformin and 2 other oral drugs is not effective, not tolerated or contraindicated, consider triple therapy by switching one drug for a GLP-1 mimetic for adults with type 2 diabetes who:

- Have a BMI ≥35 (adjust according to ethnicity) & specific psychological or other medical problems associated with obesity
- Have a BMI <35 and for whom insulin would have significant occupational implications
- Have a BMI <35 for who weight loss would benefit other significant obesity-related comorbidities
- BMI Adjustment for Obesity: White European ≥30 & Asian ≥27.5²²

- Dulaglutide 1.5 mg OW; if required maybe titrated by 1.5 mg every 4 weeks as tolerated to a maximum dose 4.5 mg OW
- S/C Semaglutide 0.25mg OW, up titrate by 0.25mg every 4 weeks to maximum dose 1 mg OW
- PO Semaglutide 3mg OD, up titrate to 7mg after 1 month, maximum dose 14 mg OD if required
- Liraglutide 0.6 mg OD, up titrate to 1.2mg after one week to maximum dose 1.2mg daily (as per NWL guidelines)

Sick Day Guidance – to be reiterated to patients at every opportunity

When unwell (acute illness):

Fever, sweats, shaking
Vomiting / diarrhoea
Unable to eat or drink

Miss out / Omit / Pause:

S – SGLT-2i
A – ACEi
D – Diuretics
M – Metformin
A – ARBs
N - NSAIDs

After 2-3 days:

Feeling better = Restart paused medicines
Not better = seek medical attention

Increase blood glucose monitoring during acute illness and check for ketones. If you are using daily insulin or an SUs, you may need to increase (or decrease) the amount taken to maintain appropriate glucose control. Ensure fluid intake to minimise dehydration.

Adapted from Imperial College Healthcare NHS Trust Renal Sick Day Rules

Lifestyle Counselling – to be reiterated to patients at every opportunity

Dietary Guidance

Seek dietitian input. Individualised approach: low fat, low carbohydrate / low Glycaemic Index diet. Alternatives include low calorie total diet replacement programmes (NWL REWIND).

Physical Activity

Realistic targets should be set. The benefits of regular exercise should be explained and people should be advised to perform regular aerobic activity. Clinical studies show that walking for 30 minutes every day has cardiovascular benefits.

Weight Management

Weight loss can help the patient achieve Type 2 diabetes remission. Realistic initial weight loss target of 5% to 10% of starting weight. Consider drug therapy, e.g SGLT-2i or GLP-1. Consider surgical intervention.

Smoking Cessation & Alcohol consumption

Assess patients for smoking status and refer to Smoking Cessation Teams for support. Alcohol may influence blood glucose control (Hyper/Hypo glycaemia respectively).

Medication review

Reassess the person's needs and circumstances at each review (3-6 months) and think about whether to stop any medicines that are not effective. Adjustments for Renal & Hepatic Impairment – see [page 15](#).

GLP-1

Only continue in those with a beneficial metabolic response after **6 months** (reduction of ≥ 11 mmol/mol [1.0%] in HbA1c and weight loss of $\geq 3\%$ of initial body weight).

SGLT-2i

Stop & reassess if complicated by active foot ulcer or DKA (could be euglycemic).

DPP-4i

Not to be used in conjunction with GLP-1.

TZD

Stop in the event of HF, DKA or bladder cancer.

SU

In the event of significant hypos, stop & reassess.

Caution should be exercised when using semaglutide in patients with diabetic retinopathy treated with insulin. In patients with diabetic retinopathy treated with insulin and semaglutide, an increased risk of developing diabetic retinopathy complications has been observed. These patients should be monitored closely and treated according to clinical guidelines.

Diabetes Remission Programme



Diabetes remission is a practical target for primary care¹. Consider enrolment into NWL REWIND Programme for either low calorie total diet replacement or low carb pathway².

[For more details, click here](#)
[For full pathways, click here](#)

MHRA update June 2022: Checking Vitamin B12 serum levels in patients treated with metformin³

Test levels in patients with symptoms suggestive of, or risk factors associated with, B12 deficiency. The risk increasing with higher doses of metformin and treatment duration.

Given the recent wealth of publications regarding cardiovascular & renal outcome trials in type 2 diabetes, this Type 2 Diabetes Management Algorithm is meant as a quick reference guide as we move away from glucose-centric prescribing, based on current evidence as of August 2020. For more in-depth guidance please refer to full [North West London Diabetes Guidelines](#), the [EASD-ADA Consensus Document](#), or other [inter]national guidelines. [Also see CaReMe multi-association position statement](#).

Lifestyle management should be part of the ongoing discussion with individuals with T2DM at each visit. Increasing physical activity and reducing body weight improves glycaemic control and should be encouraged in all people with T2DM¹. Glycaemic treatment targets should be individualised based on patient preferences and patient characteristics, including frailty and comorbid conditions¹. All drugs can cause side effects, consult BNF or summary of product characteristics for full side effect profile of individual drugs. Always offer advice on sick day guidance for patients on Metformin and/or SGLT-2i¹. Stop SGLT-2is peri-operatively or if restricted food intake or dehydration¹. Patients on insulin treatment should always be advised never to stop or significantly reduce their insulin as part of the sick day response¹. SU & TZD both have low acquisition cost, this should be taken into consideration alongside increased risk of weight gain and hypoglycaemia risk (SU).

Abbreviations:

T2DM; type 2 diabetes mellitus; NWL REWIND; North West London Reducing Weight with Intensive Dietary support, eGFR, estimated glomerular filtration rate; SGLT-2i, sodium-glucose cotransporter-2 inhibitor; DPP-4i, dipeptidyl peptidase 4 inhibitor (gliptin); SU, sulfonylurea; TZD, thiazolidinedione; BMI, body mass index; GLP-1, glucagon-like peptide-1 receptor agonist; +ive, positive; CVD, cardiovascular disease; eCVD, established cardiovascular disease; MI, myocardial infarction; HF, heart failure; CKD, chronic kidney disease with eGFR < 60; HbA_{1c}, hemoglobin A1C; BD, twice daily; ACEi, Angiotensin-converting enzyme inhibitors; ARB, Angiotensin II receptor blocker; NSAID, Non-steroidal anti-inflammatory drug; DKA, diabetic ketoacidosis; uACR, urine albumin creatinine ratio; HF_{rEF}, Heart Failure with reduced Ejection Fraction; HF_{pEF}, Heart Failure with preserved Ejection Fraction.

References:

1. DiRECT; Lancet 2018; 391: 541–51 [https://doi.org/10.1016/S0140-6736\(17\)33102-1](https://doi.org/10.1016/S0140-6736(17)33102-1)
2. NWL REWIND Programme (**R**educing **W**eight with **I**ntensive **D**ietary support) [For more details, click here](#). [For full pathways, click here](#).
3. MHRA volume 15, issue 11: June 2022: [Drug Safety Update on metformin + Vitamin B12 monitoring](#)
4. When prescribing an SGLT-2i, consider risk of volume depletion, euglycemia DKA in insulin deficient cohorts and lower limb amputation (class warning, but only observed in Cana and Eurtu). Caution in frail patients and always follow sick day rules. For more information, refer to full [North West London Diabetes Guidelines](#)
5. DECLARE TIMI 58; N Engl J Med 2019; 380:347-357; DOI: <https://doi.org/10.1056/NEJMoa1812389>
6. FDA Drug Safety Communication: FDA adds warnings about heart failure risk to labels of type 2 diabetes medicines containing saxagliptin and alogliptin <https://bit.ly/2ZZCNni>
7. TZD (Pioglitazone) to be avoided in patients with heart failure. PROactive; Lancet. 2005 Oct 8;366(9493):1279-89 [https://doi.org/10.1016/S0140-6736\(05\)67528-9](https://doi.org/10.1016/S0140-6736(05)67528-9)
8. REWIND (Dulaglutide CVOT); Lancet 2019; 394: 121–30; DOI: [https://doi.org/10.1016/S0140-6736\(19\)31149-3](https://doi.org/10.1016/S0140-6736(19)31149-3)
9. Patients with established atherosclerotic cardiovascular disease having had an ischemic event (e.g myocardial infarction or stroke)
10. Consider initiating Met + SGLT-2i rather than stepwise. This is in line with Position Statement by Primary Care Diabetes Europe; S. Seidu, et al., A disease state approach to the pharmacological management of Type 2 diabetes in primary care: A position statement by Primary Care Diabetes Europe, Prim. Care Diab. (2020), <https://doi.org/10.1016/j.pcd.2020.05.004>. Alternatively, the European Society of Cardiology (ESC) diabetes guideline states that SGLT-2i could be considered as first line ahead of metformin in patients with eCVD, HF or CKD - European Heart Journal (2019) 00, 169; doi: <https://doi.org/10.1093/eurheartj/ehz486>
11. EMPA-REG; N Engl J Med 2015; 373:2117-2128; DOI: <https://doi.org/10.1056/NEJMoa1504720>
12. CANVAS; N Engl J Med 2017; 377:644-657; DOI: <https://doi.org/10.1056/NEJMoa1611925>
13. PIONEER 6; N Engl J Med 2019; 381:841-851; DOI: <https://doi.org/10.1056/NEJMoa19011186>
14. SUSTAIN 6; N Engl J Med. 2016 Nov 10;375(19):1834-1844 DOI: <https://doi.org/10.1056/NEJMoa1607141>
15. ABCD SGLT-2i & GLP-1 Position Statement (2021) Basu, et al. *BJD*. 2021; 21(1): 132-148 <https://bit.ly/3zXBWmf>
16. DAPA HF; September 19, 2019; DOI: <https://doi.org/10.1056/NEJMoa1911303>
17. CREDENCE; N Engl J Med 2019; 380:2295-2306; DOI: <https://doi.org/10.1056/NEJMoa1811744>
18. DAPA CKD; N Engl J Med 2020; 383:1436-1446; DOI: <https://doi.org/10.1056/NEJMoa2024816>
19. EMPOROR REDUCED; N Engl J Med 2020; 383:1413-1424 DOI: <https://doi.org/10.1056/NEJMoa2022190>
20. EMPEROR-Preserved; N Engl J Med 2021; 385:1451-1461 DOI: <https://doi.org/10.1056/NEJMoa2107038>
21. NG28 [Type 2 diabetes in adults: management \(nice.org.uk\)](#)
22. [BMI: preventing ill health and premature death in black, Asian and other minority ethnic groups | Guidance | NICE](#)
23. DELIVER; N Engl J Med 2022; 387:1089-1098; DOI: <https://doi.org/10.1056/NEJMoa2206286>